**Background**

AGEN1181 is a clinical stage novel Fc- enhanced anti-CTLA-4 therapy developed to deliver:

1. Superior efficacy: Via novel Fc-mechanism that promotes enhanced T cell priming and Treg depletion
2. Improved safety: Avoid complement mediated toxicity associated with many current immune checkpoint inhibitors
3. Expand therapeutic reach by improved binding to CD16 (FcγRIIIa) for both low and high affinity allele patients

**Objectives**

**Primary**
- Access safety, tolerability, and DLT of AGEN1181 as monotherapy and in combination with AGEN2034 (anti-PD-1) in subjects with advanced solid tumors
- Determine the RP2D

**Secondary**
- Characterize the pharmacokinetic profile & immunogenicity of AGEN1181 monotherapy & combination with AGEN2034 (anti-PD-1) antibody
- To assess ORR, DOR, DCR, and PFS per RECIST 1.1

**Exploratory**
- Pharmacodynamic of AGEN1181 alone and in combination with AGEN2034
- Explore the correlation of polymorphism of fragment crystallizable gamma receptor (FcγR) expression with clinical responses and/or toxicity

**Methods**

**Key Inclusion Criteria**
1. ≥ 18 years of age
2. Histologically or cytologically confirmed diagnosis of metastatic or locally advanced solid tumor for which no standard therapy is available or standard therapy has failed
3. Measurable disease on imaging based on Response Evaluation Criteria in Solid Tumors (RECIST 1.1)
4. Life expectancy of ≥ 12 months
5. Performance status of 0 or 1
6. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

**Key Exclusion Criteria**
- Currently participating and receiving other investigational product
- Received prior systemic cytotoxic chemotherapy, biological therapy radiotherapy, or major surgery within 3 weeks prior to first dose
- Received prior therapy with an anti-CTLA-4 antibody or agent
- Known severe (Grade ≥ 3) hypersensitivity reactions to fully human monoclonal antibodies

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**Clinical Trial Status**
- **Benefit was observed in majority of patients treated with monotherapy or combination**
- Prolonged disease stabilization has been observed at low doses of AGEN1181 monotherapy
- **Clinical benefit observed in patients with poor prognosis**
- **Clinical benefit has been observed in patients with multiple tumor types**
- **AGEN1181 is designed to avoid complement mediated toxicities**
- No hypophysitis has been observed to date. The safety observations from this early phase clinical trial studies suggest improved safety compared to other anti CTLA-4 antibodies.

**Summary and Next Steps**
- AGEN1181 was Fc-engineered and designed to: Promote superior T cell priming/Activation
- Enhance Treg Depletion
- Provide safety benefits (i.e. eliminate hypophysitis)
- Broaden the patient population of responders

The AGEN1181 Phase I trial will continue through dose escalation and expansion with accelerated development in prevalent indications with limited/no effective treatment options including but not limited to PD-1-refractory small-cell lung cancer and Melanoma, MSI colorectal cancer and endometrial, and others.